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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,105	12/20/2001	Carlo Farina	P32331	7825

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EXAMINER	
LIU, HONG	
ART UNIT	PAPER NUMBER
1624	10

DATE MAILED: 08/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,105	FARINA ET AL.	
	Examiner	Art Unit	
	Hong Liu	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 16-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-8 and 16-19 are pending in this application.

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No. 9 is acknowledged. Applicants are expected to cancel the non-elected subject matter in the claims.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the United Kingdom on June 24, 1999. A copy of the priority document, however, is not found in the file.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 and 16-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for preparation of compounds wherein Y and Z are CH, CR1, or CR2, does not reasonably provide enablement for preparation and use of compounds wherein Y and Z are nitrogen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The nature of the invention in the instant application has claims which embrace a diversity of chemically and physically distinct compounds, wherein Y and Z can be an either a

nitrogen or carbon such that the core of the molecule is benzimidazole, imidazo[4,5-c]pyridine, or imidazopyrimidine, etc. While many compounds are disclosed, there is insufficient guidance for preparing additional osteoclasts inhibitors which would be effective since the cited examples are drawn to a homogenous group of compounds not remotely commensurate in scope to applicants' claims. Only compounds wherein the core is benzimidazole have been made.

Furthermore, testing data is limited to a number of compounds not considered to be representative of all the possible compounds encompassed by the claims. Examples should be of sufficient scope as to justify the scope of the claim. However, the generic claims are much broader in scope than is represented by the testing. The definitions of the various Y and Z variables embrace many structurally divergent groups not represented at all in testing, since testing for the instant compounds is not seen in the specification. Markush claims must be provided with support in the disclosure when the "working examples' fail to include written description(s) which teach how to make and use Markush members embraced thereby in full, clear and exact terms. See In re Fouch, 169 USPQ 429.

This area of activity can be expected to be highly structure specific and unpredictable, as is generally true for chemically-based pharmacological activity. In view of the structural divergence in the claims, one skilled in the art could not reasonably extrapolate the activities of some of the claimed compounds to the other structurally divergent compounds embraced by the claims which have not been tested. In cases directed to chemical compounds which are being used for their physiological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provided by the specification. See In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. No reasonable assurance has been made

that the instant compounds as an entire class have the required activities needed to practice the invention. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability" have been demonstrated to be sufficiently lacking in the instant case for the scope being claimed.

Claims 6-8 and 16-19 are drawn to a method of for the treatment of tumor, viral conditions, AIDS and angiogenic diseases, angiogenic diseases etc. However, the applicant discloses on P.1 of specification that "the therapeutic target for the selective inhibition of osteoclasts is controversial" and that V-ATPase has been identified only "as a potential therapeutic target". In a recent review article, Vasikaran wrote that potent inhibitors of osteoclast-mediated bone resorption are only useful in treating "Paget's disease of bone, j-hypercalcaemia and osteolytic bone disease of malignancy, primary and secondary hyperparathyoridism and osteoporosis. (Ann. Clin. Biochm., 2001)" Additionally, no evidence of in vitro/in vivo effectiveness is seen in the specification for one of the (let alone all) of the instant compounds for the uses claimed herein. See In re Surrey, 252 USPQ 724, regarding sufficiency of disclosure. Competent evidence of art-recognized efficacy for intended uses needs to be provided. Any evidence presented must be commensurate in scope with the claims and must clearly demonstrate the likelihood of in vivo use for all uses being claimed. See Ex parte Powers, 220 USPQ 925.

In claim 6, instant claim language embraces disorders not only for treatment but also for PREVENTION (prophylaxis) which is not remotely enabled. It is presumed in the prevention of disease and/or disorders claimed herein there is a way of identifying those people who may develop diseases associated with over activity of osteolasts. There is no evidence of record which

would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorders claimed herein.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 18, and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1). The use of "heterocyclyl" in the definition of R variables is unclear to the array of heteroatoms, size of the rings, as well as nature of atoms as ring members. See In re Wiggins 179 USPQ 421 for certain terminology regarding heterocyclic ring systems.

2). Claim 6 is of indeterminate scope for more than one reason. First, no one particular disorder is recited. Second, the claim language may read on diseases not yet fully understood to be affected by osteoclasts over-activity.

3). "Substituted or unsubstituted" throughout claim 1 is unclear as to the nature and number of substituent(s) intended.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Downing et al. (WO 95/30659). The reference teaches the compounds, compositions, and processes of

making the compounds of the invention. (See examples on page 27 and synthesis scheme on page 18).

Claims 1-3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Barraclough et al. (Eur. J. Med. Chem., 1992). Barraclough teaches the compounds and composition of the instant invention (see Compounds 4 and 15 on page 209).

Claims 1-3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by King et al. (J. Chem. Soc. Perkin Trans.1988). King teaches the compounds and composition of the instant invention (see Compound 22 on page 3382).

2. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by compounds having Beilstein RN 5988985, 6009580, 208984, 282385.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Downing et al. (WO 95/30659). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I, Col. 2 wherein Z is N or CH, X can be -C(O)-NH(CH2)- and R is piperidine which is a heterocyclyl group, etc. The compounds are taught to be useful as pharmaceutical agents. The claims differ from the

reference by reciting a specific species and/or a more limited genus than the reference. However, it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the specie of the genus would have similar properties and, thus, the same use as taught for the genus as a whole. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. See In re Susi, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in Merck & Co. V. Biocraft Laboratories, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Liu whose telephone number is 703 3065814. The examiner can normally be reached on 8:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703 308 4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703 308-4556 for regular communications and 703 3084734 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 358-1235.

Mukund J. Shah

Mukund Shah
Supervisory Patent Examiner
Art Unit 1624

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August 1, 2003